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Iudenich. V. A. 1954 O Revaktsinatsii protiv tularemii (Revaccination against tularemia. Zh Mikrobiol. Moskva No. 2 Feb. 54 p. 31-6.

The necessity of revaccination is in direct dependence on the intensity and duration of the retention of immunity after the first vaccination.

The question of the limiting length of the immunity through inoculations against tularemia has not been solved at the present time because the duration of the observation of the results of the mass prophylactic vaccination with live tularemic vaccine has not brought about enough firm conclusions. Nevertheless, all authors (Gaisky Elbert, Raibitch, Slatkovski, Olsooffieff, Maisky, et al) who have studied this question arrive at a unanimous conclusion that the post vaccination immunity of sufficient intensity can be retained for no less than 4 to 5 years (equal to the period of observation). Our observations have shown that the infection among inoculated people does not occur for a period of 4 to 5 years after the vaccination, even if the work has necessitated a contact with known infected products, Allergical reactions also exceed 4 years. This permits the conclusion, to be confirmed, that the immunity of vaccinated people is sustained for not less than 4 years. Thus revaccination of people with positive reactions is unnecessary prior to 4 years. This conclusion was inserted in the resolution of a meeting dealing with a study of the effectiveness of inoculations against tularemia held in the Ministry of Health, USSR on the 11 and 12 of June 1951 in Moscow. In accordance with the resolutions of the meeting, revaccination must be carried out in accordance with the same epidemiological indicators as were pertinent during the primary prophylactic vaccination-- that is if the positive reactions to tularemia are less than 75%.

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In accordance with our data the allergical reactions of inoculated people remains positive and therefore an immunity is retained up to 3 years in 84.2% whereas by 4 years this figure drops to 73.3%. However, taking into consideration

our experimental data which shows that the immunity in the guinea pigs which were inoculated against tularemia is retained even after the cessation of skin allergical reactions, one can assume that with people, vaccinated with live tularemic material, the lack of skin allergy would not mean a complete loss of immunity to tularemic infection. On the whole one can reckon that after 4 years following vaccination, $3/4$ of the vaccinated population would remain immune. Such immune protection guarantees against the outbreak of an epidemic. In view of this a revaccination of the population subjected to a precautionary mass vaccination with live tularemic vaccine which is active for 4 years should only be carried out in accordance with epidemic indications and after careful checking for the existence of allergical reactions.

Besides the question of the interval for revaccination and the necessity for carrying it out, a question that is extremely important is the reaction in previously inoculated persons following repeat inoculations with live tularemic preparations. This question has not been studied much up to the present time and little light is thrown on it in the literature. We had the opportunity to re-vaccinate 200 people who had been vaccinated against tularemia 3 years earlier and to observe on them the local and general reactions after the revaccination with live tularemic vaccine.

Revaccination was carried out on people in the age bracket 10 to 60 and older. Before revaccinating, the allergical reaction was checked and 56 people (were observed for(?) the presence of specific agglutination. Out of 200 vaccinated people, 170 (85%) showed positive tularemic reactions (allergical?): 32% were one plus, 33.5% were two plus, 19.5% were three plus.

From 56 tested, there were 39 (69.6%) positive in the titers of 1 to 10 and 1 to 20 and only 2 showed higher titers; one was 1:40 and the other 1:80.

17 people showed a negative agglutination reaction. The cited percentages of positive allergic and serological reactions almost completely coincided with the percentages previously observed when a study of the vaccinated people against tularemia was made 3 years earlier. In that series an allergic reaction was observed in 884.2% and an agglutination reaction was present in 61.2% of cases.

The skin vaccination of liquid tularemic vaccine of the Smolensk Institute of Epidemiology and Microbiology was performed on all 200 people who were reactive or non-reactive to tularensis as shown by application of the subcutaneous test. After the vaccination (revaccination) 188 of them showed a local cutaneous reaction. The development of a local reaction on the sensitive and non sensitive individuals was different.

Out of 170 people who reacted positively on the diagnostic test, 142 showed a cutaneous reaction to the tularemic vaccine after (?) 24 to 48 hours with the reaction subsiding after 4 to 5 days..

The reaction was characterized by the formation of an infiltration around the scarification site and by a reddening of varied intensity. The outside appearance and the time it took to appear resembled cutaneous allergic reaction to tularemia. We are inclined to believe that the local vaccination cutaneous process develops in accordance with the type of allergic reaction (which is encountered).

In 19 people (11.2%) the cutaneous reaction was manifested in a different manner: After revaccination there was a reddening and an infiltration after 24 hours. By the 4th or 5th day, little blisters appeared which dried up rapidly and formed small scabs which remained until the 10th to 12th day following vaccination. The remaining 9 revaccinated people (5.3%) depending upon the local cutaneous reaction proved (to be) negative. A somewhat different picture was observed on revaccinated people with a negative allergic reaction. Out of 30 such people, 19 (exhibited) a spreading cutaneous reaction after

vaccinating with live tularemic vaccine. Similarly, in the ones who were vaccinated for the first time, swelling and reddening of the vaccination site occurred between the 6th and 10th day. The entire vaccination process, with dropping of the scabs, was over after 3 to 4 weeks. With 8 people a premature cutaneous reaction appeared at 48 hours after the vaccination and the accelerated duration of the process was completed by the 10th to 12th day. With 3 people there was no reaction on the vaccination site when they were revaccinated. What appeared outstanding with this group of people was that they did not register the type of cutaneous reaction after revaccination which we estimated as an allergical one with the first group of revaccinated people.

It is necessary to assume that in those people who show a cutaneous reaction after revaccination, the response is similar to that which follows the first vaccination, i.e., there is a complete loss of the allergical reactivity and immunity previously derived from the vaccination.

In studying the actual reaction, of greatest interest are those with the shortened cycle of duration which were observed with 8 revaccinated people who had negative allergical tests. There is no basis to consider them strongly allergically reactive as it is hard to assume that people who did not react to a subcutaneous injection of tularin would give a violent allergical reaction to a live, attenuated culture through the skin. It would be more correct to diagnose this type of reaction as an accelerated response of vaccinated people who have lost a high intensity immunity but who have left over traces of past resistance.

Out of 200 revaccinated people we had the opportunity to observe a general reaction to revaccination in 142. Comparative data on these general reactions of people previously vaccinated & revaccinated are shown on table I.

TABLE I

Group under observation	No.	Indisposed headache	Temperature rise 37.2-37.8° C	Pain in Arm Pits	Swelling of Lymphatic Glands	Disability
Ist Vaccination	15,862	8.7%	5.2%	3.1%	2.2%	0%
Revaccinated after 3 years	112	6.3%	4.8%	18.3%	12.7%	1.4%

It is to be noted that during revaccination the expressed reaction in regard to swelling of lymphatic glands was greater than the reaction after the 1st vaccination and the general reaction expressed by general disability, headaches and rise in temperature, was in a small percentage but was more severe and in some cases brought about loss of working capacity by the 2nd or 3rd day which was not observed with the group who were vaccinated for the first time.

Kasberook revaccinated 63 who had been vaccinated with tularemic vaccine 3 yrs & 10 mos previously & noted that the local reaction during revaccination progressed faster and were less pronounced than during the primary vaccination. In checking a month after the revaccination all vaccinated people showed traces of local reaction in the form of drying scabs. Peeling or ridging of the epithelium occurred during scarification. From this we can conclude that with all revaccinated persons a local skin process following the vaccination occurred in a similar manner as during the 1st vaccination. Unfortunately the allergical reaction was not checked by the author prior to the revaccination. Hence it is unknown whether or not an immunity existed at the time of revaccination. During the meeting of the Health Ministry of the USSR held between the 11 & 12th June 1951 in Moscow, Ooglovoy quoted comparative data on the general reaction of 408 individuals vaccinated for the first time and 112 people revaccinated after 1 year. In accordance with his data the revaccinated people had less complaints about indisposition & headaches but showed noticeably more lymphadenopathy up to 50.9%

against 15.4% with the people vaccinated for the 1st time & also a more than double increase in disability--3.8% with the 1st vaccination vs. 9.5% with the revaccinated. It is pointed out that Ooglovoy shows a considerable percentage of overall reactions (31.6%), lymphadenopathy 15.4%, and disability (3.8%) with the people vaccinated on the skin with tularemic vaccine. We have not noticed such high reactivity after vaccination with liquid tularemic vaccine which was performed on the majority. In regard to the higher reactivity observed by Ooglovoy on the re-vaccination-- 1 yr after the primary vaccination.

All above mentioned data proves that people who are vaccinated with tularemic vaccine retain a positive allergy reaction whereby there is noted a higher reactivity of the lymphatic barrier during the secondary introduction of specific antigen & whereby the strength of the reaction & frequency of its manifestations appear in direct proportion with the intensity of the immunity.

As general severe reactions, lymphadenopathy and loss of working capacity is more frequent in revaccinated people than in people vaccinated for the first time, one must exercise a certain caution in order to avoid undesirable complications. The reactivity invasiveness of the organism during the secondary vaccination, 3 to 4 yrs after the 1st vaccination becomes more moderate.

In studying revaccination we had the opportunity to observe the progress of the vaccination process in people who had tularemia 2 to 8 years previously. Only 33 people were observed. They were vaccinated in 1950. Out of them 24 people were vaccinated with liquid and 9 with dry tularemic on the skin, vaccine.

The stipulated intracutaneous allergical reaction prior to the vaccination was positive (+ + + with 21, + + with 7, & + with 5 people). The majority of people under observation showed an allergical reaction with a large infiltration and noticeable hyperemia, with 10 people were noted a small increase of the lymphatic glands in the arm pits and 6 people complained of a malaise. The agglutination reaction with everybody was positive in a titer of 1:10 to 1:80.

The cited results allow the assumption that the previously infected people had a well expressed immunity to tularemia.

The reaction after the vaccination carried out on these people had a character similar to the revaccinated people but was accompanied with more pronounced manifestation of malaise.

The local skin reaction after vaccination with 28 people appeared after 24 to 48 hrs & terminated by the 5th to 7th day, with 3 the skin reaction which appeared after 48 hrs continued for 10 days.

TABLE II

Group under Observation	No.	Generally Indisposed, Headaches	Temp Rise	Pain in Arm Pits	Swelling of lymph glands	Disability
Vaccinated 1st	15,862	8.7%	5.2%	3.1%	2.2%	0
Revaccinated	142	6.3%	4.8%	18.3%	12.7%	1.4%
previously infected)	33	8 People	3 People	9 People	7 People	1 Person
		24.2%	9%	27.2%	21%	3%

It is obvious in observing the data contained in the 2nd table that people who had previously been infected react to vaccination with live tularemia with greater sensitivity which in its nature is an intensely expressed allergy to the intra-cutaneous tularemic virus but there was a delayed spreading of the vaccination process. The basis of this conclusion shows a noticeable similarity to the vaccinated reaction with the test of tularin: an early appearance of local skin reaction, its cessation, as quoted, of the same duration as with the tularemic test and its overall reaction whose general character resembles the reaction of the people undergoing the tularemic test.

With the decrease of the intensity of immunity, the skin reaction to tularin is considerably lessened or completely vanishes. We have observed this on guinea pigs. We could observe this on people who were vaccinated 3 to 4 yrs. prior. The stronger the immunity, the more pronounced the skin reaction to tularemia.

The tularemic vaccine has not to a lesser extent all characteristics of the allergin than tularin which is used with the allergical test hence it is natural that people who had been infected 2 to 8 years prior & who maintain a high percentage of acquired immunity when vaccinated show an outstanding allergical reaction to the intracutaneous tularemic vaccine.

CONCLUSIONS

- 1 The necessity of revaccination among a large percentage of population must be determined by the condition of immunity of the vaccinated people and to the epidemiological evidence for specific prophylactic.
2. A firm retention of immunity caused by vaccination against tularemia during 4 to 5 yrs basically proves that the revaccination should not be carried out prior to that period. In case epidemiological evidence requires vaccination of the population, where mass vaccination had been previously carried out, an allergy test of immunity must be made and should negative reaction of more than 25% of the vaccinated appear, revaccination should be carried out.
3. When the revaccination is carried out 3 yrs after the primary local skin vaccination the vaccination process with 83.5% of the revaccinated people occurs as an allergic reaction. With people who were previously vaccinated & lost the allergy reaction, the revaccination process in its progress & duration entirely corresponds in most cases with the progress of the primary vaccination process.
4. With a part of the revaccinated, non-reacting to tularin or exhibiting a weak allergic reaction to the local skin test, the vaccination develops itself similar to a curtailed vaccinator reaction (duration).
5. With people who retain a positive allergic reaction after the 1st vaccination, revaccination is accompanied with an increase in the incidence of general reactions & a loss of capacity to work of 1.20.
6. The skin vaccination with live tularemic vaccine on people who have been infected previously shows a character of a pronounced allergic reaction & progresses with a considerable percentage of overall reactions, swelling of the lymphatic glands & loss of work capability in a minor number of cases.